

INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 227/03621	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/IL 03/00533	International filing date (day/month/year) 25.06.2003	Priority date (day/month/year) 25.06.2002
International Patent Classification (IPC) or both national classification and IPC A61B5/00		
Applicant GLUCON INC. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

- I Basis of the opinion
- II Priority
- III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV Lack of unity of invention
- V Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI Certain documents cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

Date of submission of the demand 22.01.2004	Date of completion of this report 13.09.2004
Name and mailing address of the International preliminary examining authority:  European Patent Office - Gitschner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	Authorized Officer Abraham, V Telephone No. +49 30 25901-563



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I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-19 as originally filed

Claims, Numbers

1-18 filed with telefax on 22.08.2004

Drawings, Sheets

1/9-9/9 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

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5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).
(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)
6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-18
	No: Claims	
Inventive step (IS)	Yes: Claims	1-18
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-18
	No: Claims	

2. Citations and explanations

see separate sheet

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Reference is made to the following documents:

- D1: WO 00 62659 A (SNOW BRENT W ;CARTWRIGHT PATRICK C (US); MANSFIELD JOHN T (US)) 26 October 2000 (2000-10-26)
- D2: LARIN K ET AL: 'MONITORING OF TEMPERATURE DISTRIBUTION IN TISSUES WITH OPTOACOUSTIC TECHNIQUE IN REAL TIME' PROCEEDINGS OF THE SPIE, SPIE, BELLINGHAM, VA, US, vol. 3916, 25 January 2000 (2000-01-25), pages 311-321, XP008008329 ISSN: 0277-786X
- D3: SEIP R ET AL: "NONINVASIVE ESTIMATION OF TISSUE TEMPERATURE RESPONSE TO HEATING FIELDS USING DIAGNOSTIC ULTRASOUND" IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, IEEE INC. NEW YORK, US, vol. 42, no. 8, 1 August 1995 (1995-08-01), pages 828-839, XP000556811 ISSN: 0018-9294

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1. The combination of the features of claim 1 is neither known from, nor rendered obvious by, the available prior art.

Document D1 discloses a tissue monitor comprising a heat source and means for non invasively determining the temperature development inside the tissue in order to determine tissue viability (page 5, lines 23-35). It may be obvious to use photoacoustical spectroscopy for non invasive temperature measurement as defined for example in document D2 (see abstract). However, the additional feature according to which the concentration of an analyte is also determined photoacoustically, thereby improving the accuracy of the measurement, is neither known from nor rendered obvious by, the available prior art. Thus, the subject-matter of claim 1 meets the requirements of Article 33(2)-(4) PCT.

- 1.1 Claims 2- 16 are dependent on claim 1 and therefore also meet the requirements of Article 33(2)-(4) PCT.
2. The combination of the features of claim 17 is neither known from, nor rendered obvious by, the available prior art.

Document D1 discloses a tissue monitor comprising a heat source and means for non invasively determining the temperature development inside the tissue in order to determine tissue viability (page 5, lines 23-35). It may be obvious to use conventional diagnostic ultrasound for non invasive temperature measurement as defined for example in document D3 (see abstract). However, the additional

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feature according to which the concentration of an analyte is determined photoacoustically, thereby improving the accuracy of the measurement, is neither known from nor rendered obvious by, the available prior art. Thus, the subject-matter of claim 17 meets the requirements of Article 33(2)-(4) PCT.

- 2.1 Claims 18 is dependent on claim 17 and therefore also meets the requirements of Article 33(2)-(4) PCT.
3. The independent claims should have been drafted in the two part form in accordance with Rule 6.3(b) PCT, with those features known in combination from D1 being placed in the preamble (Rule 6.3(b)(i) PCT) and with the remaining features being included in a characterising part (Rule 6.3(b)(ii) PCT).
4. The features of the claims should have been provided with reference signs placed in parentheses (Rule 6.2(b) PCT).
5. According to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D3 should have been mentioned in the description and these documents should have been identified therein.

CLAIMS

1. A tissue viability monitor (TVM) for determining viability of a biological tissue comprising:
 - 5 at least one light source controllable to illuminate the tissue with light that generates photoacoustic waves therein;
 - at least one acoustic transducer that generates signals responsive to the photoacoustic waves; and
 - a controller that receives the signals and processes the signals to determine at least one characteristic of the tissue and a measure of viability responsive to the determined at least one characteristic.
- 10
2. A TVM in accordance with claim 1 wherein the controller processes the signals to determine locations of sources of the photoacoustic waves within the tissue.
- 15
3. A TVM in accordance with claim 2 wherein the locations of sources of photoacoustic waves are determined with a resolution equal to or better than about 100 micrometers.
4. A TVM in accordance with claim 2 wherein the locations of sources of photoacoustic waves are determined with a resolution equal to or better than about 50 micrometers.
- 20
5. A TVM in accordance with claim 2 wherein the locations of sources of photoacoustic waves are determined with a resolution equal to or better than about 20 micrometers.
- 25
6. A TVM in accordance with any of the preceding claims wherein the at least one characteristic of the tissue comprises a concentration of at least one analyte.
7. A TVM in accordance with claim 6 wherein the at least one analyte is a plurality of analytes.
- 30
8. A TVM in accordance with claim 6 or claim 7 wherein the at least one analyte comprises the redox state cytochrome a,a3.

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9. A TVM in accordance with any of claims 6-8 wherein the at least one analyte comprises Hydrogen ions.

10. A TVM in accordance with any of claims 6-9 wherein the at least one analyte
5 comprises hemoglobin.

11. A TVM in accordance with any of claims 6-10 wherein the at least one analyte comprises oxygenated hemoglobin.

10 12. A TVM in accordance with any of the preceding claims and comprising a heat pump that the controller controls to generate a temperature difference between the tissue and an ambient temperature of surrounding tissue and wherein the at least one characteristic comprises a relaxation time characteristic of a time period during which the temperature difference relaxes to zero.

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13. A TVM in accordance with claim 12 wherein the heat pump comprises an acoustic transducer of the at least one acoustic transducer, which the controller controls to transmit acoustic waves to the tissue that generate the temperature difference.

20 14. A TVM in accordance with claim 12 or claim 13 wherein to determine the relaxation time the light source illuminates the tissue with light at a wavelength at which light is absorbed by water to generate photoacoustic waves in the tissue and the controller uses the signals generated by the at least one transducer to determine temperature of water in the tissue and thereby of the tissue.

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15. A TVM in accordance with any of claims 12-14 wherein the controller determines temperature of the tissue during generation of the temperature difference to monitor the generation of the temperature difference.

30 16. A TVM in accordance with claim 15 wherein the controller controls the heat pump responsive to the determined temperature.

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17. A TVM according to any of the preceding claims and comprising a catheter having a probe end that is positioned in a neighborhood of or in contact with the tissue to determine tissue viability and wherein the light source comprises an optic fiber having an optic end located at the probe end from which optic end light that illuminates the tissue is radiated.

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18. A TVM in accordance with claim 17 wherein the at least one at least one acoustic transducer comprises at least one acoustic transducer mounted in the probe end of the catheter.

10 19. A tissue viability monitor (TVM) for determining viability of a biological tissue comprising:

a heat pump controllable to non-invasively generate a temperature difference between the tissue and an ambient temperature of surrounding tissue; means for non-invasively determining a temperature of the tissue; and

15 a controller that determines from the determined temperature a relaxation time characteristic of a time period during which the temperature difference relaxes to zero.

20 20. A TVM in accordance with claim 19 wherein the heat pump comprises an acoustic transducer, which the controller controls to transmit acoustic waves to the tissue that generate the temperature difference.

25 21. A TVM in accordance with claim 19 or claim 20 wherein the means for non-invasively determining a temperature of the tissue comprises means for non-invasively determining a temperature of water in the tissue.

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22. A TVM in accordance with any of claims 19-21 wherein the means for determining a temperature of the water comprises:

a light source controllable to illuminate the tissue with light which is absorbed by the water and generates photoacoustic waves in the tissue;

30 at least one acoustic transducer that generates signals responsive to the photoacoustic waves; and

a controller that receives the signals and processes the signals to determine the temperature of the water.

23. A TVM in accordance with any of claims 19-21 wherein the means for determining a temperature of the water comprises:

- an acoustic transducer that transmits acoustic waves that are incident on the tissue;
- 5 an acoustic transducer that generates signals responsive to acoustic waves scattered from the transmitted waves by the tissue;

a controller that receives the signals and determines a characteristic of the scattered acoustic waves which it uses to determine temperature of the tissue.

- 10 24. A TVM according to claim 23 wherein the characteristic is a frequency shift of the scattered acoustic waves relative to a fundamental acoustic frequency of the structure of the tissue.

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ART 34 AMDT